

=> b ca
 COST IN U.S. DOLLARS
 FULL ESTIMATED COST

SINCE FILE TOTAL
 ENTRY SESSION
 0.15 0.15

=> s porcine(w)TSH(w)receptor?
 32105 PORCINE
 18985 TSH
 531340 RECEPTOR?
 L1 19 PORCINE(w)TSH(w)RECEPTOR?

=> d 11 1 all

L1 ANSWER 1 OF 19 CA COPYRIGHT 2002 ACS

AN 131:350079 CA

TI The interaction of TSH receptor autoantibodies with 125I-labelled TSH
 receptor

AU Sanders, Jane; Oda, Yasuo; Roberts, Sara; Kiddie, Angela; Richards, Tonya;
 Bolton, Jane; McGrath, Vivienne; Walters, Susannah; Jaskolski, Donat;
 Furmaniak, Jadwiga; Smith, Bernard Rees

CS FIRS Laboratories, RSR Ltd., Cardiff, CF4 5DU, UK

SO J. Clin. Endocrinol. Metab. (1999) 84(10), 3797-3802

CODEN: JCEMAZ; ISSN: 0021-972X

PB Endocrine Society

DT Journal

LA English

CC 15-3 (Immunochemistry)

Section cross-reference(s): 2, 14

AB Detergent-solubilized ***porcine*** ***TSH*** ***receptor***
 (TSHR) has been labeled with ^{125}I using a monoclonal antibody to the
 C-terminal domain of the receptor. The ability of sera contg. TSHR
 autoantibody to immunoppt. the labeled receptor was then investigated.
 Sera neg. for TSHR autoantibody (as judged by assays based on inhibition
 of labeled TSH binding to detergent-solubilized porcine TSHR) immunopptd.
 about 4% of the labeled receptor, whereas sera with high levels of
 receptor autoantibody immunopptd. more than 25% of the labeled receptor.
 The ability to immunoppt. labeled TSHR correlated well with ability of the
 sera to inhibit labeled TSH binding to the receptor ($r = 0.92$; $n = 63$),
 and this is consistent with TSHR autoantibodies in these samples being
 directed principally to a region of the receptor closely related to the
 TSH binding site. Preincubation of labeled TSHR with unlabeled TSH before
 reaction with test sera inhibited the immunopptn. reaction, providing
 further evidence for a close relationship between the TSHR autoantibody
 binding site(s) and the TSH binding site. This was the case whether the
 sera had TSH agonist (i.e., thyroid stimulating) or TSH antagonist (i.e.,
 blocking) activities, thus, providing no clear evidence for different
 regions of the TSHR being involved in forming the binding site(s) for TSHR
 autoantibodies with stimulating and with blocking activities. The ability
 of TSHR autoantibodies to stimulate cAMP prodn. in isolated porcine
 thyroid cells was compared with their ability to immunoppt. labeled
 porcine TSHR. A significant correlation was obsd. ($r = 0.58$; $n = 50$; $P <$
 0.001) and the correlation was improved when stimulation of cAMP prodn.
 was compared with inhibition of labeled TSH binding to porcine TSHR ($r =$
 0.76). Overall, the authors' results indicate that TSHR autoantibodies
 bind principally to a region on the TSHR closely related to the TSH
 binding site, and this seems to be the case whether the autoantibodies act
 as TSH agonists or antagonists.

ST TSH receptor autoantibody ligand binding site

IT Blood serum

Graves' disease

(TSH receptor autoantibodies bind principally to region on TSH receptor
 closely related to TSH binding site in various human sera)

IT Thyrotropin receptors

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(TSH receptor autoantibodies bind principally to region on TSH receptor
 closely related to TSH binding site in various human sera)

IT Antibodies

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(autoantibodies, monoclonal; TSH receptor autoantibodies bind
 principally to region on TSH receptor closely related to TSH binding
 site in various human sera)

IT Thyroid gland, disease

(autoimmune thyroiditis; TSH receptor autoantibodies bind principally to region on TSH receptor closely related to TSH binding site in various human sera)

IT Protein motifs
(ligand binding site; TSH receptor autoantibodies bind principally to region on TSH receptor closely related to TSH binding site in various human sera)

IT Lupus erythematosus
(systemic; TSH receptor autoantibodies bind principally to region on TSH receptor closely related to TSH binding site in various human sera)

IT 9002-71-5, TSH
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(TSH receptor autoantibodies bind principally to region on TSH receptor closely related to TSH binding site in various human sera)

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (2) Asahi, K; Clin Endocrinol Jpn (Hormone to Rynsho) 1996, v44, P401
- (3) Costagliola, S; J Clin Endocrinol Metab 1999, v84, P90 CA
- (4) Davies, T; J Clin Endocrinol Metab 1998, v83, P3777 CA
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- (6) Hoyer, D; Trends Pharmacol Sci 1993, v14, P270 CA
- (7) Kasagi, K; J Clin Endocrinol Metab 1982, v54, P108 CA
- (8) Neve, K; Biochem Soc Trans 1995, v23, P112 CA
- (9) Oda, Y; J Mol Endocrinol 1998, v20, P233 CA
- (10) Prentice, L; J Clin Endocrinol Metab 1997, v82, P1288 CA
- (11) Rapoport, B; Endocr Rev 1999, v19, P673
- (12) Rees Smith, B; Endocr Rev 1988, v9, P106 MEDLINE
- (13) Sanders, J; Bailliere's Clin Endocrinol Metab 1997, v11, P451 MEDLINE
- (14) Southgate, K; Clin Endocrinol 1984, v20, P539 CA
- (15) Strange, P; Trends Pharmacol Sci 1996, v17, P238 CA
- (16) Worthington, J; Clin Endocrinol 1991, v34, P147 MEDLINE
- (17) Wortsman, J; J Clin Endocrinol Metab 1998, v83, P2302 CA

=> d 11 2-19 all

L1 ANSWER 2 OF 19 CA COPYRIGHT 2002 ACS

AN 129:184445 CA

TI Effect of solubilization of porcine thyrotropin (TSH) receptor on TSH binding and on radio-receptor assay for anti-TSH receptor antibodies

AU Watanabe, Yukihiko; Tada, Hisato; Hidaka, Yoh; Takano, Toru; Amino, Nobuyuki

CS Department of Laboratory Medicine, Osaka University Medical School, Suita, 565-0871, Japan

SO Biochem. Biophys. Res. Commun. (1998), 248(1), 110-114

CODEN: BBRCA9; ISSN: 0006-291X

PB Academic Press

DT Journal

LA English

CC 2-5 (Mammalian Hormones)

AB The effect of solubilization of ***porcine*** ***TSH*** ***receptor*** (TSHR) on TSH binding and on the radio-receptor assay for anti-TSHR antibodies was exampd. After TSHR solubilization with 1% dodecylpolyethyleneglycoether, TSH binding affinity was increased, from K_d = 1.15nM to 0.45nM, and TSH binding capacity was slightly increased, from 0.15nM to 0.19nM. With a particulate membrane suspension from thyroid cells, blocking of TSH binding to the membrane suspension by anti-TSH receptor antibody was obsd. only for thyroid stimulation blocking antibody (TSBAb), not for thyroid-stimulating antibody (TSAb). After the solubilization of TSHR, both TSBAb and TSAb blocked TSH-binding to the solubilized TSHR. The authors speculate that TSAb interacts with the TSHR in the native conformation without interfering with TSH binding, and that after the solubilization, any anti-TSHR antibody interferes with TSH-binding due to the conformational change in TSHR. With these particulate thyroid cell membrane prepns., the authors can detect only TSBAb by the radio-receptor assay. (c) 1998 Academic Press.

ST TSH receptor binding solubilization antibody

IT Immunoglobulins

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(TSH binding-inhibiting; effect of solubilization of ***porcine*** ***TSH*** ***receptor*** on TSH binding and on radio-receptor assay for anti-TSH receptor antibodies)

IT Solubilization

(Effect of solubilization of ***porcine*** ***TSH***

receptor on TSH binding and on radio-receptor assay for anti-TSH receptor antibodies)

IT Thyrotropin receptors

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(effect of solubilization of ***porcine*** ***TSH***
receptor on TSH binding and on radio-receptor assay for anti-TSH receptor antibodies)

IT 9002-71-5, Thyrotropin

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(effect of solubilization of ***porcine*** ***TSH***
receptor on TSH binding and on radio-receptor assay for anti-TSH receptor antibodies)

L1 ANSWER 3 OF 19 CA COPYRIGHT 2002 ACS

AN 129:53347 CA

TI Receptor binding assay for detection of TSH-receptor antibodies as well as reagents for its execution

IN Bergmann, Andreas; Struck, Joachim
PA B.R.A.H.M.S Diagnostica G.m.b.H., Germany
SO Ger. Offen., 12 pp.

CODEN: GWXXBX

DT Patent

LA German

IC ICM G01N033-543
ICS G01N033-78; G01N033-68

CC 15-1 (Immunochemistry)

Section cross-reference(s): 2, 14

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19651093	A1	19980610	DE 1996-19651093	19961209
	DE 19651093	C2	19990610		
	WO 9826294	A1	19980618	WO 1997-EP6767	19971203
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 943098	A1	19990922	EP 1997-952034	19971203
	R: AT, BE, CH, DE, FR, IT, LI				
	JP 2001505999	T2	20010508	JP 1998-526179	19971203
PRAI	DE 1996-19651093	A	19961209		
	WO 1997-EP6767	W	19971203		

AB The invention concerns a competitive immunoassay for the improved diagnosis of Morbus Basedow by detecting TSH-receptor autoantibodies from human serum. The method includes parts of the known TRAK Assay. The analyte TSH-receptor antibodies are competing for the TSH-receptor with labeled TSH primary competitor and with a secondary competitor, that consists of an antibody against a peptide fraction of the TSH-receptor. The peptide fraction is typical for Morbus Basedow and the usage of the monoclonal antibody against it improves the sensitivity of the assay. The TSH-receptor is of human, animal or recombinant origin, the competing assay is carried out on a solid surface, that are particles, small tubes, microtiter plates from glass or plastic. Thus monoclonal antibody was raised against the peptide comprising the amino acid sequence 20-29 of the human TSH-receptor, the antibody was immobilized onto Carbolink Gel and filled into a column. Test soln., ***porcine*** ***TSH***
receptor, radioactive iodine labeled TSH were mixed, incubated and loaded onto the column contg. the secondary competitor bound to the solid phase. After rinsing the column the radioactivity of the column was measured. For calcns. a std. curve was established as given for the com. available TRAK-Assay.

ST TSH receptor autoantibody detn competitive immunoassay; Morbus Basedow TSH receptor autoantibody RIA; Graves disease diagnosis TRAK assay

IT Blood analysis

Graves' disease

Immobilization (animal)

RIA (radioimmunoassay)

Serum (blood)

(competitive RIA for the detection of TSH-receptor autoantibodies in Morbus Basedow disease)

IT Autoantibodies

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(competitive RIA for the detection of TSH-receptor autoantibodies in Morbus Basedow disease)

IT Thyrotropin receptors

RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (uses)

(competitive RIA for the detection of TSH-receptor autoantibodies in

IT Morbus Basedow disease)
Monoclonal antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(competitive RIA for the detection of TSH-receptor autoantibodies in
Morbus Basedow disease)
IT Immunoassay
(competitive; competitive RIA for the detection of TSH-receptor
autoantibodies in Morbus Basedow disease)
IT 129290-72-8, Carbolink Gel 145848-98-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(competitive RIA for the detection of TSH-receptor autoantibodies in
Morbus Basedow disease)

L1 ANSWER 4 OF 19 CA COPYRIGHT 2002 ACS

AN 128:57761 CA

TI Human thyrotropin receptor compositions and use thereof

IN ~~Rapoport, Basil~~; McLachlan, Sandra
PA Rapoport, Basil, USA; McLachlan, Sandra
SO PCT Int. Appl., 152 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K

CC 2-1 (Mammalian Hormones)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9746206	A2	19971211	WO 1997-US9624	19970605
	W: AU, CA, JP			RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE	
	CA 2258720	AA	19971211	CA 1997-2258720	19970605
	AU 9733762	A1	19980105	AU 1997-33762	19970605
	EP 959896	A2	19991201	EP 1997-929783	19970605
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	JP 2000512280	T2	20000919	JP 1998-500809	19970605
	US 1996-19171	P	19960605		
	WO 1997-US9624	W	19970605		

AB TSH receptor compns. and methods of use are disclosed, useful for
diagnostic and therapeutic purposes. Thus, human TSH receptor can be used
in a TSH binding inhibition (TBI) assay for TSH receptor autoantibodies.
The efficacy of the solubilized human and ***porcine*** ***TSH***
receptor was compared in a TBI assay using sera from 30
individuals with known or suspected Graves' disease. Ten of these sera
had undetectable TSH receptor autoantibodies when ***porcine***
TSH ***receptor*** was used. The TBI values obtained when
human TSH receptor was used correlated very well with values detd. with
TSH receptor ($r = 0.954$). However, 2 sera that were neg. with
porcine ***TSH*** ***receptor*** antigen were pos. with
the human TSH receptor. Therefor, one aspect of the present disclosure is
the improvement assays for the detection of TSH receptor autoantibodies.
Two cleavage sites were detected in the human TSH receptor. Evidence is
also presented that high level expression of human TSH receptor in CHO
cells is assocd. with neg. cooperativity among TSH receptors in terms of
their affinity for ligand. Carboxy-terminal truncation of the human TSH
receptor ectodomain generates a secreted protein with complex carbohydrate
that neutralizes autoantibodies in Graves' disease patients' sera. This
antigenically active TSH receptor truncated form is useful for the
diagnosis, pathogenesis, and immunotherapy of Graves' disease.

ST TSH receptor Graves disease; autoantibody TSH receptor Graves disease

IT Graves' disease

(human TSH receptor diagnostic and therapeutic and autoregulatory
activity and cleavage sites)

IT Thyrotropin receptors

RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)

(human TSH receptor diagnostic and therapeutic and autoregulatory
activity and cleavage sites)

IT Immunodiagnosis

(human TSH receptor immunodiagnostic uses)

IT Immunotherapy

(human TSH receptor immunotherapeutic uses)

IT Blood analysis

(human TSH receptor in detn. of TSH receptor autoantibodies)

IT Autoantibodies

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL

(Biological study); USES (Uses)

(to TSH receptor; human TSH receptor diagnostic and therapeutic and autoregulatory activity and cleavage sites)

IT 9002-71-5, Thyrotropin

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(human TSH receptor diagnostic and therapeutic and autoregulatory activity and cleavage sites)

L1 ANSWER 5 OF 19 CA COPYRIGHT 2002 ACS

AN 122:76067 CA

TI Competitive binding assay method and its use in determination of serum autoantibodies to TSH receptors

IN Bergmann, Andreas; Struck, Joachim; Kornfeld, Shaul

PA Henning Berlin GmbH, Germany

SO Ger., 14 pp.

CODEN: GWXXAW

DT Patent

LA German

IC ICM G01N033-53

ICS G01N033-78; C12Q001-00

CC 9-10 (Biochemical Methods)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4328070	C1	19941124	DE 1993-4328070	19930820
	WO 9506258	A1	19950302	WO 1994-EP2748	19940818
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 724726	A1	19960807	EP 1994-925460	19940818
	EP 724726	B1	19971105		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 09500215	T2	19970107	JP 1994-507334	19940818
	AT 160023	E	19971115	AT 1994-925460	19940818
	US 5814461	A	19980929	US 1996-596172	19960709
PRAI	DE 1993-4328070		19930820		
	WO 1994-EP2748		19940818		

AB An analyte is detd. in a liq. sample by (a) adding a predetd. amt. of a binding partner (B1) for the analyte, (b) adding a predetd. amt. of a labeled or labelable competing reagent (K) which also binds to B1, (c) simultaneously or subsequently incubating the reaction mixt. with a solid phase coated with a 2nd binding partner (B2) for selective immobilization of unbound K, (d) quant. sepn. of phases, and (e) detn. of the immobilized label on K. This method was applied to detn. of autoantibodies to TSH receptors in serum of patients with Graves' disease, using ***porcine*** ***TSH*** ***receptors*** as B1, bovine TSH as K, a monoclonal antibody to TSH bound to the wall of the assay tube as B2, and a 2nd monoclonal antibody to TSH labeled with an acridinium ester as labeling reagent for the immobilized TSH.

ST TSH receptor autoantibody competitive binding assay; immunoassay TSH receptor autoantibody serum

IT Blood analysis

Immunoassay

(competitive binding assay method and use in detn. of serum autoantibodies to TSH receptors)

IT Graves' disease

(diagnosis; competitive binding assay method and use in detn. of serum autoantibodies to TSH receptors)

IT Receptors

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (TSH, competitive binding assay method and use in detn. of serum autoantibodies to TSH receptors)

IT Antibodies

RL: ANT (Analyte); ANST (Analytical study) (auto-, competitive binding assay method and use in detn. of serum autoantibodies to TSH receptors)

IT Antibodies

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (monoclonal, to TSH; competitive binding assay method and use in detn. of serum autoantibodies to TSH receptors)

IT 9002-71-5, Thyrotropin

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (competitive binding assay method and use in detn. of serum autoantibodies to TSH receptors)

L1 ANSWER 6 OF 19 CA COPYRIGHT 2002 ACS

AN 118:73911 CA

TI Molecular cloning of a cDNA fragment for porcine thyrotropin receptor
AU Shi, Yufei; Zou, Minjing; Farid, Nadir R.; Berbue, Dominique
CS Health Sci. Cent., Mem. Univ. Newfoundland, St. John's, NF, Can.
SO Prog. Thyroid Res., Proc. Int. Thyroid Conf., 10th (1991), 99-102.
Editor(s): Gordon, Amirav; Gross, Jack; Hennemann, Georg. Publisher:
Balkema, Rotterdam, Neth.
CODEN: 58JYAY
DT Conference
LA English
CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 3
AB A 500-bp transmembrane region of ***porcine*** ***TSH***
receptor cDNA was cloned and used to det. the gene copy no. as
well as human chromosomal location of the gene.
ST TSH receptor cDNA cloning
IT Molecular cloning
(of TSH receptor cDNA)
IT Receptors
RL: BIOL (Biological study)
(TSH, cDNA for, mol. cloning of)
IT Deoxyribonucleic acid sequences
(complementary, for TSH receptor)
IT 9002-71-5, TSH
RL: BIOL (Biological study)
(receptor for, cDNA for, mol. cloning of)

L1 ANSWER 7 OF 19 CA COPYRIGHT 2002 ACS

AN 114:56045 CA

TI Biological activity and metabolic clearance of a recombinant human
thyrotropin produced in Chinese hamster ovary cells
AU Thotakura, N. Rao; Desai, Rajesh K.; Bates, Lisa G.; Cole, Edward S.;
Pratt, Bruce M.; Weintraub, Bruce D.
CS Mol., Cell. Nutr. Endocrinol. Branch, Natl. Inst. Diabetes Dig. Kidney
Dis., Bethesda, MD, 20892 USA

SO Endocrinology (Baltimore) (1991), 128(1), 341-8

182

QP187. A1 JF

Serial

CODEN: ENDOAO; ISSN: 0013-7227

DT Journal

ADONIS 128(1)

LA English

CC 2-5 (Mammalian Hormones)

AB The presence and specific structures of the oligosaccharides on TSH have
been shown to be important for its prodn. and bioactivity. Since the
carbohydrate structure of a protein reflects the glycosylation app. of the
host cells in which the protein is expressed, the biol. activity and
metabolic clearance of a prepn. of purified recombinant human (rh) TSH
derived from a stable transfectant of Chinese hamster ovary cells were
examd. Carbohydrate compositional anal. of this rTSH showed it to be more
highly sialylated than a nonrecombinant, cadaver-derived pituitary hTSH.
In addn., no N-acetyl galactosamine was detectable in rTSH, which implies
the absence of terminal sulfate moieties, both of which are present in
pituitary-derived TSH. The immunol. activity and ***porcine***
TSH ***receptor*** -binding activity of the prepn. of rTSH
were 3-4-fold lower than those of a std. pituitary hTSH. The rTSH showed
a max. stimulatory activity similar to that of pituitary hTSH in 2
different in vitro bioassays. However, rTSH elicited about 3-fold and
5-fold less cAMP than pituitary TSH after stimulation of adenylyl cyclase
in bovine thyroid membranes and the rat FRTL-5 cell line, resp. Removal
of sialic acid did not alter the immunol. activity of rTSH. However, the
potencies of rTSH in receptor-binding, adenylyl cyclase, and FRTL-5
assays were increased 2.4-, 2.6-, and 26.7-fold, resp. after sialic acid
removal. These data suggest that the in vitro biol. activity of rTSH is
influenced by its highly sialylated oligosaccharide chains. The rTSH had
a 2-fold lower metabolic clearance rate than pituitary TSH, resulting in a
greater than 10-fold higher serum concn. of rTSH at 3 h as compared to
pituitary hTSH. After sialic acid removal, the rTSH was cleared faster
(7.5-fold) than pituitary hTSH, showing that its longer plasma half-life
was due to its higher sialylation. Biol. active rTSH should be of clin.
value in the diagnosis and treatment of patients with thyroid cancer and
as a pure hTSH ref. prepn.

ST TSH sialic acid bioactivity metab

IT Sialic acids

RL: BIOL (Biological study)
(of TSH, recombinant human, bioactivity and metabolic clearance rate in
CHO cells in relation to)

IT 9002-71-5, TSH

RL: BIOL (Biological study)
(bioactivity and metabolic clearance rate of recombinant human, in CHO
cells, sialic acid content in relation to)

L1 ANSWER 8 OF 19 CA COPYRIGHT 2002 ACS

AN 111:129334 CA

TI Lutropin receptor and thyrotropin receptor share a common epitope
AU Bedin, C.; Antonicelli, F.; Jallal, B.; Salesse, R.; Bidart, J. M.; Remy, J. J.

CS Hopital Cochin, Paris, 75674, Fr.

SO Mol. Cell. Endocrinol. (1989), 65(1-2), 135-44

CODEN: MCEND6; ISSN: 0303-7207

DT Journal

LA English

CC 6-3 (General Biochemistry)

Section cross-reference(s): 2

AB The existence of common epitopes between 2 receptors of the glycoprotein hormone family, LH and TSH receptors, was investigated by an immunol. approach. High responder mice were immunized with purified porcine LH receptors obtained by successive affinity chromatogs. on agarose-human chorionic gonadotropin (hCG) gels. From 1 fusion of splenocytes with the murine myeloma NS1, secreting hybridomas were tested for their anti-LH receptor specificities. During sequential selection for this activity including direct recognition of the purified LH receptors in dot-blot assays and displacement expts. of ^{125}I -labeled pLH and ^{125}I -labeled hCG binding to different sources of receptors, a parallel investigation of their anti- ***porcine*** ***TSH*** ***receptor*** activities was performed. Purified Ig's from 2 of them showed a TSH-like activity on the iodide metab. of porcine thyroid cells, this activity being related to the phosphoinositide breakdown pathway; moreover, these antibodies obtained after immunization with porcine LH receptors were able to immunopurify human TSH receptors. The double selection process led to the characterization of 3 groups of Ig's: exclusive specificities for lutropin receptors or TSH receptors and cross-reactive specificities. The results demonstrate the possibility of sequence homologies at the protein and the gene levels between the receptors for the glycoprotein hormone family supporting the hypothesis of a common origin in evolution.

ST receptor LH TSH common epitope

IT Receptors

RL: BIOL (Biological study)

(for LH and TSH, common epitope of)

IT 9002-71-5, TSH

RL: BIOL (Biological study)

(receptors for, LH receptor common epitope with)

IT 9002-67-9, LH

RL: BIOL (Biological study)

(receptors for, TSH receptor common epitope with)

L1 ANSWER 9 OF 19 CA COPYRIGHT 2002 ACS

AN 108:69416 CA

TI About the ***porcine*** ***TSH*** ***receptor***

AU Farid, Nadir R. Fahraeus-Van Ree, Goverdina

CS Thyroid Res. Lab., Health Sci. Cent., St. John's, NF, A1B 3V6, Can.

SO Acta Endocrinol. (Copenhagen), Suppl. (1987), 115(281), 181-5

CODEN: ACEDAB; ISSN: 0300-9750

DT Journal

LA English

CC 2-7 (Mammalian Hormones)

AB Using a no. of immunol. and biochem. approaches, a no. of $[^{125}\text{I}]$ bTSH binding peptides with Mr .apprx.45,000, 66,000-70,000, .apprx.95,000 were identified; larger conjugates capable of binding the hormone have not been excluded. A conservative interpretation of the data suggest a basic receptor unit of Mr .apprx.95,000 of which Mr 45,000 and 66,000-70,000 are proteolytic products of membrane-bound proteases. The assocn. of 2 intact subunits by strong noncovalent forces may generate >3 TSH binding sites.

ST thyroid hormone receptor binding protein

IT Thyroid gland, composition

(TSH-binding peptides of cell nuclei of)

IT Proteins, specific or class

RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)

(TSH-binding, of thyroid gland)

IT 9002-71-5, TSH

RL: BIOL (Biological study)

(receptors of, of thyroid nucleus, binding peptides in relation to)

L1 ANSWER 10 OF 19 CA COPYRIGHT 2002 ACS

AN 106:832 CA

TI Assessment of the shape and molecular size of TSH-TSH receptor complexes

AU Furmaniak, J.; Jones, E. Davies; Buckland, P. R.; Howells, R. D.; Smith,

B. Rees
CS Coll. Med., Univ. Wales, Cardiff, CF4 4XN, UK
SO Mol. Cell. Endocrinol. (1986), 48(1), 31-8
CODEN: MCEND6; ISSN: 0303-7207
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB Section cross-reference(s): 6
Photoaffinity labeling and anal. under denaturing conditions (SDS-PAGE) have shown that the ***porcine*** ***TSH*** ***receptor*** contains an A subunit (mol. wt. (Mr) = 47,000) which forms the binding site for TSH and a B subunit (Mr = 25,000) linked to the A subunit by a ss bridge. To assess the size and shape of the receptor under nondenaturing conditions, photoaffinity-labeled ***porcine*** ***TSH*** ***receptors*** were solubilized with the small micelle-sized detergent Na deoxycholate and the preps. were analyzed by sucrose-d. gradient centrifugation and gel filtration. Under these conditions, the cross-linked TSH-TSH receptor complex showed a sedimentation value of 6.4 S and a frictional ratio (f/f₀) of 1.8. These values were consistent with those which might be expected from an elongated protein complex with a mol. wt. of apprx. 100,000 (the value obtained by SDS-PAGE). Anal. of another thyroid membrane protein, human thyroid microsomal antigen (Mr = 110,000 by SDS-PAGE) under the same conditions gave a sedimentation value of 6.0 S and f/f₀ = 1.3, which suggests that this protein has a compact structure. The TSH receptor A subunit cross-linked to TSH (Mr = 70,000 by SDS-PAGE) gave a sedimentation value of 4.6 S and f/f₀ = 1.8, and these values could be compared with those obtained for the A subunit alone (3.6 S; f/f₀ = 1.4; Mr by SDS-PAGE = 47,000) and TSH alone (2.6 S; f/f₀ = 1.6; Mr = 28,000). Thus, when TSH (which has an elongated structure) combines with the TSH receptor A subunit (which has a compact structure), the 2 proteins do not fold into each other extensively but form a structure with an even greater degree of elongation.

ST TSH receptor complex size shape
IT Receptors

IT RL: BIOL (Biological study)
(for thyrotropin, mol. size and shape of)

IT 9002-71-5D, TSH, receptor complexes

IT RL: BIOL (Biological study)
(mol. size and shape of)

L1 ANSWER 11 OF 19 CA COPYRIGHT 2002 ACS
AN 105:112803 CA

TI TSH receptor antibody induction of thyroglobulin release from human thyroid cell monolayers

AU Feldman, A.; Schwartz, A. E.; Friedman, E. W.; Davies, T. F.
CS Dep. Med., Mount Sinai Sch. Med., New York, NY, 10029, USA
SO Clin. Endocrinol. (Oxford) (1986), 25(1), 45-53
CODEN: CLECAP; ISSN: 0300-0664

DT Journal
LA English

CC 13-6 (Mammalian Biochemistry)

AB Section cross-reference(s): 2, 14

The influence of TSH receptor antibody (TRA), as detected by inhibition of ¹²⁵I-bovine(b) TSH binding to detergent solubilized ***porcine*** ***TSH*** ***receptors***, on *in vitro* human thyroglobulin (hTg) prodn. was exmd. using normal thyroid cells in monolayer. Secretion of hTg into the culture medium was analyzed by a noncompetitive ELISA technique utilizing 2 murine monoclonal antibodies. Basal hTg release [124 ng/105 cells/6 day(d)] was stimulated by bTSH (10, 102, 103 .mu.unit/mL) in a dose-related manner (191, 587, 695 ng/105 cells/6 d, resp.). IgG (2 mg/mL) from patients with hyperthyroid Graves' disease, and known titers of TRA, similarly enhanced prodn. of hTg, in a dose and time-dependent manner when compared with control IgG. The degree of induction varied, with 140-230% increases in total hTg release over a 6-d incubation. There was a direct correlation between the degree of ¹²⁵I-bTSH binding inhibitory activity and the hTg response. Thus, TSH receptor antibodies enhance hTg release from human thyroid cell monolayers and allow an assessment to be made of antibody-activated post receptor mechanisms.

ST TSH receptor antibody thyroglobulin thyroid; Graves disease TSH receptor antibody; Ig Graves disease thyroglobulin prodn

IT Graves' disease

IT (Igs from, thyroglobulin prodn. by thyroid cells from human stimulation by)

IT Receptors

IT RL: BIOL (Biological study)

IT (for thyrotropin, antibodies to, thyroglobulin prodn. by thyroid cells

IT of human stimulation by)
Thyroglobulins
RL: FORM (Formation, nonpreparative)
(formation of, by thyroid cell culture from human, thyrotropin receptor antibody stimulation of)
IT Thyroid gland, metabolism
(thyroglobulin prodn. by cell culture from human, TSH receptor antibodies stimulation of)
IT Antibodies
RL: BIOL (Biological study)
(to TSH receptor, thyroglobulin release from human thyroid cell cultures induction by)
IT Immunoglobulins
RL: BIOL (Biological study)
(G, from Graves' disease patients, thyroglobulin prodn. by thyroid cells of humans stimulation by)
IT 9002-71-5
RL: BIOL (Biological study)
(receptors for, antibodies to, thyroglobulin prodn. by thyroid cells of human stimulation by)

L1 ANSWER 12 OF 19 CA COPYRIGHT 2002 ACS

AN 102:215647 CA

TI Immunoprecipitation of TSH-TSH receptor complexes
AU Parkes, A. B.; Kajita, Y.; Buckland, P. R.; Howells, R. D.; Rickards, Carole R.; Creagh, Fionuala M.; Rees Smith, B.
CS Coll. Med., Univ. Wales, Cardiff, CF4 4XN, UK
SO Clin. Endocrinol. (Oxford) (1985), 22(4), 511-20
CODEN: CLECAP; ISSN: 0300-0664

DT Journal

LA English

CC 2-5 (Mammalian Hormones)

AB Section cross-reference(s): 14

The ability of Graves' sera to interact with the TSH receptor crosslinked to a ^{125}I -labeled photoactive deriv. of TSH was investigated. Crosslinked complexes were prepnd. using nonpurified detergent-solubilized human thyroid and guinea pig fat TSH receptors. Affinity-purified ***porcine*** ***TSH*** ***receptor*** preps. were also used. After crosslinking, the crosslinked TSH-TSH receptor complexes were sepd. from aggregates and free TSH on Sephadryl S-300 and incubated with test sera followed by immunopptn. using anti-IgG or Protein A. Using nonpurified human TSH receptors crosslinked to TSH, a mean of 12.1% of the crosslinked complex was immunopptd. with Graves' sera compared with 10.3 with Hashimoto sera and 3.8% with normal sera. These values were markedly reduced when TSH receptor preps. free of other thyroid autoantigens (guinea pig fat TSH receptors) were used. Under these conditions immunopptn. with Graves' sera was 1.6% compared with 0.8% for Hashimoto sera and 0.8% for normal sera. Addn. complexes formed between TSH and affinity-purified ***porcine*** ***TSH*** ***receptors*** gave low immunopptn. values for Graves' (1.44%) and Hashimoto sera (1.7%) which were not significantly different. Overall, therefore, the effects of Graves' and Hashimoto sera were similar and the amts. of material immunopptd. were markedly reduced when TSH receptor preps. contg. reduced amts. of other autoantigens were used. Consequently, the Graves' sera did not appear to interact specifically with crosslinked TSH-TSH receptor complexes. However, the Graves' sera did contain TSH receptor antibodies which could inhibit the binding of labeled TSH to TSH receptors in the preps. used and these results suggest that the binding of TSH and these antibodies to the receptor is mutually exclusive.

ST TSH binding receptor antibody Graves

IT Receptors

RL: BIOL (Biological study)
(TSH complexes, antibodies of blood serum in Graves disease interaction with, of human and lab. animals)

IT Graves' disease

(Antibodies of blood serum in, TSH-receptor complexes of human and lab. animals interaction with)

IT Thyroid gland, disease or disorder

(Hashimoto's, antibodies of blood serum in, TSH-receptor complexes of human and lab. animals interaction with)

IT 9002-71-5D, receptor complexes

RL: BIOL (Biological study)
(Antibodies of blood serum in Graves disease interaction with, of human and lab. animals)

L1 ANSWER 13 OF 19 CA COPYRIGHT 2002 ACS

AN 102:143331 CA

TI A structure for the ***porcine*** ***TSH*** ***receptor***
AU Kajita, Yoshihiro; Rickards, Carole R.; Buckland, Paul R.; Howells, Roger
D.; Smith, Bernard Rees
CS Coll. Med., Univ. Wales, Cardiff, CF4 4XN, UK
SO FEBS Lett. (1985), 181(2), 218-22
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 6
AB Affinity purified, detergent-solubilized porcine thyroid gland TSH [9002-71-5] receptors were crosslinked to a ^{125}I -labeled photoactive deriv. of TSH and analyzed by gel electrophoresis, gel filtration, and sucrose d. gradient centrifugation. Apparently, ***porcine*** ***TSH*** ***receptor*** is made up of a hydrophilic A subunit with a mol. wt. (Mr) of .apprx.45,000 linked to an amphiphilic B subunit (Mr .apprx.25,000) by a disulfide bridge(s). The A subunit forms the binding site for TSH on the outside of the cell membrane. The B subunit appears to penetrate the membrane and form the site for interaction with adenylate cyclase [9012-42-4] either in the lipid bilayer or close to the cytoplasmic surface of the membrane.
ST TSH receptor structure; thyroid TSH receptor structure; adenylate cyclase
TSH receptor structure
IT Cell membrane
(TSH receptors of, of thyroid gland, structure of)
IT Thyroid gland, composition
(TSH receptors of, structure of)
IT Receptors
RL: BIOL (Biological study)
(for TSH, of thyroid gland, structure of)
IT Conformation and Conformers
(of TSH receptor, of thyroid gland)
IT 9012-42-4
RL: BIOL (Biological study)
(TSH receptor conformation in thyroid gland in relation to)
IT 9002-71-5
RL: BIOL (Biological study)
(receptors for, structure of)
IT 9002-71-5D, receptor complexes
RL: PRP (Properties)
(structure of, of thyroid gland cell membranes)
L1 ANSWER 14 OF 19 CA COPYRIGHT 2002 ACS
AN 102:125884 CA
TI Affinity-labeling of the thyrotropin receptor. Characterization of the photoactive ligand
AU Buckland, Paul R.; Howells, Roger D.; Rickards, Carole R.; Rees Smith, Bernard
CS Endocrine Immunol. Unit, Welsh Natl. Sch. Med., Cardiff, CF4 4XN, UK
SO Biochem. J. (1985), 225(3), 753-60
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 6, 9
AB TSH was coupled to the photoactive heterobifunctional reagent N-hydroxysuccinimidyl 4-azidobenzoate (HSAB) and the properties of the product (HSAB-TSH) investigated. Preps. of HSAB-TSH contg. 2 mols. of HSAB per mol. of TSH were used in most expts. and these preps. retained .apprx.40% of the original receptor-binding activity of the TSH. HSAB-TSH could be labeled with ^{125}I and crosslinked to porcine and human TSH receptors. Anal. of the crosslinked complexes indicated that the receptors consisted of 2 subunits (designated A and B) linked by a disulfide bridge. In the case of the human TSH receptor, the A- and B-subunits had approx. mol. wt. (Mr) values of 50,000 and 30,000, resp., whereas the Mr values for ***porcine*** ***TSH*** - ***receptor*** A- and B-subunits were .apprx.45,000 and 25,000, resp. Only the A subunit was crosslinked to TSH. Comparison suggested that the trypsin cleavage point on the A-subunit was at a point close to the disulfide bridge.
ST TSH receptor characterization; hydroxysuccinimidyl azidobenzoate TSH receptor
IT Receptors
RL: BIOL (Biological study)
(for TSH, characterization of, hydroxysuccinimidylazidobenzoate-TSH affinity labeling in relation to)
IT 9002-71-5D, reaction products with hydroxysuccinimidylazidobenzoate 53053-08-0D, reaction products with TSH

RL: BIOL (Biological study)
(TSH receptor affinity labeling with, characterization in relation to)

L1 ANSWER 15 OF 19 CA COPYRIGHT 2002 ACS
AN 101:921 CA

TI A receptor assay for the measurement of TSH receptor antibodies in unextracted serum

AU Southgate, Kay; Creagh, Fionuala; Teece, Michelle; Kingswood, C.; Smith, B. Rees

CS Dep. Med., Welsh Natl. Sch. Med., Cardiff, CF4 4XN, UK

SO Clin. Endocrinol. (Oxford) (1984), 20(5), 539-48

CODEN: CLECAP; ISSN: 0300-0664

DT Journal

LA English

CC 2-1 (Mammalian Hormones)

Section cross-reference(s): 14

AB A receptor assay for TSH [9002-71-5] receptor antibodies is described in which unextd. serum, detergent solubilized TSH receptors, and ^{125}I -labeled TSH are used. The assay was rapid and reproducible with relative std. deviations of 12.3, 2.1, and 2.6% at mean inhibition of TSH binding values of 11, 53, and 79 resp. Assay sensitivity was increased by reducing the vol. of receptors used but some increase in the scatter of values obtained with individual normal sera was also obsd. Comparison of human and ***porcine*** ***TSH*** ***receptor*** preps. indicated that porcine tissue gave greater sensitivity. Anal. of different groups of patients and normal subjects showed the absence of detectable TSH receptor antibody activity in patients with rheumatoid arthritis, with multinodular goiter, and with Hashimoto's disease. However, the antibody was readily detectable in Graves' patients (treated and untreated) who were hyperthyroid at the time of assay.

ST serum TSH receptor antibody detn; Graves disease TSH receptor antibody

IT Blood analysis

(TSH receptor antibodies detn. in human, by receptor assay)

IT Graves' disease

(TSH receptor antibodies of blood serum in, in humans)

IT Receptors

RL: BIOL (Biological study)

(for TSH, antibodies to, detn. of, in blood serum of humans by receptor assay)

IT Antibodies

RL: PROC (Process)

(to TSH receptor, detn. of, in blood serum of humans by receptor assay)

IT 9002-71-5

RL: BIOL (Biological study)

(receptors for, antibodies to, detn. of, in blood serum of humans by receptor assay)

L1 ANSWER 16 OF 19 CA COPYRIGHT 2002 ACS

AN 100:48020 CA

TI Molecular-weight determinations of the thyrotropin receptor by affinity labeling

AU Buckland, P. R.; Rickards, Carole R.; Howells, R. D.; Davies Jones, Eirian; Rees Smith, B.

CS Dep. Med., Welsh Natl. Sch. Med., Cardiff, CF4 4XN, UK

SO Biochem. Soc. Trans. (1983), 11(2), 189-90

CODEN: BCSTB5; ISSN: 0300-5127

DT Journal

LA English

CC 9-8 (Biochemical Methods)

Section cross-reference(s): 2

AB By using the photoreactive bifunctional reagent N-hydroxysuccinimide 4-azidobenzoate to crosslink ^{125}I -linked TSH to its receptor protein, it was found that TSH receptors in human and porcine thyroid and guinea pig fat probably contain a similar basic unit which binds one mol. of TSH. Variations in the size of the receptor were obsd. between species and a model is presented for the basic unit of the ***porcine*** ***TSH*** ***receptor***. The receptor may also contain addnl. components noncovalently linked to the basic unit.

ST TSH receptor affinity labeling

IT Receptors

RL: ANST (Analytical study)

(for TSH, affinity labeling of, mol. wt. in relation to)

IT 9002-71-5

RL: ANST (Analytical study)

(receptor for, affinity labeling of, mol. wt. in relation to)

L1 ANSWER 17 OF 19 CA COPYRIGHT 2002 ACS

AN 96:193786 CA
TI Evidence that the porcine thyrotropin (TSH) receptor contains an essential
disulfide bridge
AU Ginsberg, Jody; Rees Smith, Bernard; Hall, Reginald
CS Dep. Med., Welsh Natl. Sch. Med., Cardiff, CF4 4XN, UK
SO Mol. Cell. Endocrinol. (1982), 26(1-2), 95-102
CODEN: MCEND6; ISSN: 0303-7207
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB The effects of reducing agents on membrane-bound and detergent-solubilized porcine TSH [9002-71-5] receptors were investigated. Both 2-mercaptoethanol and dithiothreitol appeared to inhibit the TSH-binding activity by a direct effect on the TSH receptor itself and Scatchard anal. suggested that this was primarily due to an alteration in TSH-binding capacity. In addn., some binding activity could be recovered by reoxidn. of reduced receptor prepns. Apparently, the ***porcine*** ***TSH*** ***receptor*** contains an essential disulfide bridge.

ST TSH receptor disulfide bridge
IT Receptors
RL: BIOL (Biological study)
(for TSH, disulfide bridges of)
IT Bond
(sulfur-sulfur, of TSH receptor)
IT 9002-71-5
RL: BIOL (Biological study)
(receptors for, disulfide bridges of)

L1 ANSWER 18 OF 19 CA COPYRIGHT 2002 ACS

AN 94:77129 CA
TI Evidence that the thyrotropin receptor contains at least one essential
disulfide bridge
AU Ginsberg, J.; Rees Smith, B.; Hall, R.
CS Dep. Med., Univ. Wales, Cardiff, CF4 4XN, Wales
SO J. Endocrinol. (1980), 87(2), 33P-34P
CODEN: JOENAK; ISSN: 0022-0795

DT Journal
LA English
CC 2-1 (Hormone Pharmacology)

AB The reducing agents, 2-mercaptoethanol and dithiothreitol, dose-dependently inhibited ^{125}I -labeled TSH [9002-71-5] binding to membrane-bound and detergent-solubilized ***porcine*** ***TSH*** ***receptors***. Recovery of TSH binding was obsd. following removal of reducing agent or addn. of H_2O_2 . Thus, the ***porcine*** ***TSH*** ***receptor*** contains at least one disulfide bridge which, once reduced, is capable of undergoing partial reoxidn.

ST TSH receptor disulfide bridge
IT Receptors
RL: BIOL (Biological study)
(for TSH, disulfide bridges of)
IT Disulfide group
(of TSH receptor)
IT 9002-71-5
RL: BIOL (Biological study)
(receptor for, disulfide bridges of)

L1 ANSWER 19 OF 19 CA COPYRIGHT 2002 ACS

AN 89:173982 CA
TI Solubilization and partial characterization of human and porcine thyrotropin receptors
AU Dawes, P. J. D.; Petersen, V. B.; Rees Smith, B.; Hall, R.
CS Dep. Med., Univ. Newcastle upon Tyne, Newcastle upon Tyne, Engl.
SO J. Endocrinol. (1978), 78(1), 89-102
CODEN: JOENAK; ISSN: 0022-0795

ADONIS

DT Journal
LA English
CC 2-1 (Hormone Pharmacology)
AB Triton X-100 was used to solubilize TSH [9002-71-5] receptors from human and pig thyroid membranes and both sets of receptors had a mol. wt. of apprx. 50,000 and were assocd. with Triton micelles of mol. wt. apprx. 300,000. Human TSH receptors were heat labile, showed optimum TSH binding at pH 7.4 and reduced hormone binding at high ionic strength, and had an isoelec. point of pH 4-4.5. The binding characteristics of membrane-bound and solubilized receptors were similar and both gave curved Scatchard plots, unlike the corresponding ***porcine*** ***TSH*** ***receptors***, which gave linear plots with assocn. consts. of 2.8 times 109 and 1.7 times 109 L/mol, resp. ^{125}I -labeled TSH apparently

interacts specifically and reversibly with sol. exts. of human and porcine thyroid membranes.

ST TSH receptor thyroid membrane

IT Thyroid gland
(TSH receptor of membrane of)

IT Cell membrane
(TSH receptor of, of thyroid gland)

IT Receptors
RL: BIOL (Biological study)

(for TSH, of thyroid gland membrane)

IT 9002-71-5

RL: BIOL (Biological study)

(receptors for, of thyroid gland membrane)

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